LOW ADENOSINE ANTI-SENSE OLIGONUCLEOTIDE, COMPOSITIONS, KIT & METHOD FOR TREATMENT OF AIRWAY DISORDERS ASSOCIATED WITH BRONCHOCONSTRICTION, LUNG INFLAMMATION, ALLERGY(IES) & SURFACTANT DEPLETION

ABSTRACT OF THE INVENTION

An in vivo method of selectively delivering a nucleic acid to a target gene or mRNA, comprises the topical administration, e. g. to the respiratory system, of a subject of a therapeutic amount of an oligonucleotide (oligo) that is anti-sense to the initiation codon region, the coding region, the 5' or 3' intron-exon junctions or regions within 2 to 10 nucleotides of the junctions of the gene, or antisense to a mRNA complementary to the gene in an amount effective to reach the target polynucleotide and reducing or inhibiting expression. In addition a method of treating an adenosine mediated effect, comprises topically administering to a subject an anti-sense oligo in an amount effective to treat the respiratory, pulmonary, or airway disease. In order to minimize triggering adenosine receptors by their metabolism, the administered oligos have a low content of or are essentially free of adenosine. A pharmaceutical composition and formulations comprise the oligo anti-sense to an adenosine receptor, genes and mRNAs encoding them, genomic and mRNA flanking regions, intron and exon borders and all regulatory and functionally related segments of the genes and mRNAs encoding the polypeptides, their salts and mixtures. Various formulations contain a requisite carrier, and optionally other additives and biologically active agents. The low adenosine or adenosine free (des-A) agent for practicing the method of the invention may be prepared by selecting a target gene(s), genomic flanking region(s), RNA(s) and/or polypeptide(s) associated with a disease(s) or condition(s) afflicting lung airways, obtaining the sequence of the mRNA(s) corresponding to the target gene(s) and/or genomic flanking region(s), and/or RNAs encoding the target polypeptide(s), selecting at least one segment of the mRNA which may be up to 60% free of thymidine (T) and synthesizing one or more anti-sense oligonucleotide(s) to the mRNA segments which are free of adenosine (A) by substituting a universal base for A when present in the oligonucleotide. The agent may be prepared by selection of target nucleic acid sequences with GC running stretches, which have low T content, and by optionally replacing A in the anti-sense oligonucleotides with a "Universal or alternative base". The agent, composition and formulations are used for prophylactic, preventive and therapeutic treatment of ailments associated with impaired respiration, lung allergy(ies) and/or inflammation and depletion lung surfactant or surfactant hypoproduction, such as pulmonary vasoconstriction, inflammation, allergies, allergic rhynitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction. The present treatment is suitable for administration in combination with other treatments, e.g. before, during and after other treatments, including radiation, chemotherapy, antibody therapy and surgery, among others. Alternatively, the present agent is effectively administered prophylactically or therapeutically by itself for conditions without known therapies or as a substitute for therapies exhibiting undesirable side effects. The treatment of this invention may be administered directly into the respiratory system of a subject so that the agent has direct access to the lungs, or by other effective routes of administration, e. g. topically, transdermally, by implantation, etc., in an amount effective to reduce or inhibit the symptoms of the ailment.